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10/039,383	01/08/2002	Hsien-Juc Chu	AM100249	3951

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1645

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 10/039,383	Applicant(s) Chu et al.
Examiner S. Devi, Ph.D.	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on Aug 7, 2002

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-18 is/are pending in the application.

4a) Of the above, claim(s) 1-9 and 18 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 10-17 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

4) Interview Summary (PTO-413) Paper No(s). _____

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 246.

6) Other:

DETAILED ACTION

Election

- 1) Acknowledgment is made of Applicants' election filed 08/07/02 (paper no. 4), with traverse, of invention II, claims 10-17, in response to the restriction requirement mailed 07/08/02 (paper no. 3).

Applicants' traversal is on the grounds that the central aspect of all the claims is the preparation of a vaccine and its use to protect an animal from disease, and that a search directed to the claimed method would extend to the relevant areas of classification that covers the non-elected claims drawn to a vaccine. Applicants cite parts of M.P.E.P 802.01, 808.02 and 803 and discuss restriction as related to independent inventions, patentable distinctness and search burden.

Applicants' arguments have been carefully considered, but are non-persuasive. In the instant case, the restriction requirement follows all appropriate statutes and regulatory principles and conforms closely with guidelines provided by MPEP, Chapter 800. With regard to burden, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed, and (2) a serious *and examination* burden is placed on the Examiner if restriction is not required. Applicants are correct that the term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, for example as product and method of use, but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (MPEP 802.01). However, in the instant case, the product of invention I is capable of separate use, i.e., a non-vaccine use as a diagnostic reagent. As set forth in the restriction requirement mailed 07/08/02 (paper no. 3), invention I and invention II are related as product and process of using the product. M.P.E.P 806.05(h) permits separation of the two inventions if the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process of using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P 806.05(h)). In the instant case, the *Mycoplasma hyopneumoniae* of invention I can be used in a materially different, non-immunization process, for example, an *in vitro* diagnostic test as a coating antigen. Applicants have not presented any

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arguments showing that the claimed product cannot be used in a materially different non-immunization process.

With regard to burden of search and examination, MPEP 803 states that a burden can be shown if the Examiner shows either separate classification, different filed of search or separate status in the art. In the instant application, a burden has been established by showing that inventions I and II are classified under separate subclasses necessitating separate and non-coextensive searches of issued US patents under subclasses 93.4 as well as 263.1 of class 424. Applicants should note that divergent classification or subclassification has traditionally been utilized as one indicator that burden exists sufficient to warrant restriction. The classification system has no statutory recognition as to whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions. Further, it should be noted that the non-patent literature search, particularly in this art, is non-coextensive. Clearly, different searches and issues are involved in the examination of each invention. For these reasons, the restriction set forth in the Office Action Action mailed 07/08/02 (paper no. 3) is proper and is hereby made FINAL.

Had Applicants elected the product claims (invention I), the method of using the product claims (invention II) would have been kept pending pursuant to the rejoinder provisions of M.P.E.P 821.04 and would have been rejoined with the elected product claims if and when the latter were deemed allowable.

Status of Claims

2) Claims 1-18 are pending.

Claims 10-17 have been elected via the election filed 08/07/02.

Claims 1-9 and 18 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

The elected claims 10-17 are under examination. An Action on the Merits for these claims is issued.

Information Disclosure Statements

3) Acknowledgment is made of Applicants' Information Disclosure Statements filed 01/08/02

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(paper no. 2) and 09/20/02 (paper no. 6). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 7).

Specification - Informalities

4) The specification is objected to for the following reason(s):

(a) The use of the trademark in the instant specification has been noted in this application. For example, see page 9, line 18: "Tween 20"; page 7, line 25: "Tween 80"; page 7, lines 22 and 24 and page 12, line 10: "Pluronic L121"; page 5, line 23: "Carbopol 934P"; and page 9, line 13; page 10, line 10; page 11, line 1: "Immulon II". The recitation should be capitalized wherever it appears and be accompanied by the generic terminology. Each letter of the trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix I. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to trademark recitations, wherever such recitations appear.

(b) Some of the bacterial names recited in the first full paragraph on page 3 of the specification are misspelled: "*Haemonphilus*"; "... *multiocida*"; and "*Streptococcum*".

Rejection(s) under 35 U.S.C § 112, Second Paragraph

5) Claims 10-17 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 10 is incorrect in the recitation "pharmaceutical acceptable carrier" (see line 7). To obviate the rejection, it is suggested that Applicants replace the limitation with --pharmaceutically acceptable carrier--.

(b) Claims 11 and 12 are vague and confusing in the use of an abbreviated recitation "MHDCE" in the claim language (see line 2), because it is unclear what does this abbreviation mean or represent. It is suggested that Applicants use the full terminology at first occurrence in the claim(s), with the abbreviation retained in parenthesis.

(c) Claims 11 and 12 lack antecedent basis for the recitation "said bacteria" (see lines

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1 and/or 2). Claims 11 and 12 depend from claim 10, which does not recite any ‘bacteria’.

(d) Claim 16 is indefinite and/or incorrect in the recitation: “selected from the group of”. It is suggested that Applicants use the proper Markush language: --selected from the group consisting of--.

(e) Claim 17 is spelling-wise incorrect in the recitation: “*Haemophilus*”; “*multiocida*”; and “*Streptococcum*”. Correction is requested.

(f) Claim 17 is redundant in the recitation: “leptospira bacteria”. It is suggested that Applicants delete the limitation “bacteria” since the limitation is unnecessary.

(g) Claim 13 is confusing in the recitation “the mode of administration of said administering step”. It is suggested that Applicants replace the recitation with --the route of administration--.

(h) Claims 11-17, which depend from claim 10, are also rejected as being indefinite, because of the vagueness or indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 112, First Paragraph

6) Claims 10-17 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a method for inducing significantly reduced average lung lesions in a porcine animal administered intramuscularly with MHDCE along with Squalane/Pluronic L121 mixture and 2% W/V Carbopol, i.e., test vaccine A, when challenge-infected with 1.0×10^6 *Mycoplasma hyopneumoniae* by intratracheal administration, does not reasonably provide enablement for a method for protecting any animal against *Mycoplasma hyopneumoniae* disease comprising administering any *Mycoplasma hyopneumoniae* bacterin other than MHDCE by any route other than the intramuscular route, as claimed broadly. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

The instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);

- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant application, the claimed method is required to induce protection in any animal against a broadly recited *Mycoplasma hyopneumoniae* bacterin after a single administration along with the recited adjuvant mixture by any route. The recitation “*Mycoplasma hyopneumoniae* bacterin” encompasses any bacterin of *Mycoplasma hyopneumoniae*, i.e., those that have been predetermined to be protective and those that have not been pre-demonstrated to be protective. The recitation “animal” encompasses any animal, a vertebrate or a non-vertebrate, a mammalian or a non-mammalian, and a human or a non-human animal. Claim 13 recites the mode of administration of the vaccine composition to be intramuscular, subcutaneous, intraperitoneal, aerosol, oral or intranasal. However, the full scope of the instant claims is not enabled. In the instant application, the only *Mycoplasma hyopneumoniae* bacterin that has been shown to significantly decrease the average lung lesion score exclusively in a porcine animal after a single administration by intramuscular route when given along with the recited adjuvant mixture followed by challenge-infection with 1.0×10^6 *Mycoplasma hyopneumoniae* is *Mycoplasma hyopneumoniae* DNA cell equivalents (MHDCE). See Example 4. No other *Mycoplasma hyopneumoniae* bacterin other than the MHDCE-containing Test Vaccine A administered by no other route other than the intramuscular route in no other animals other than pigs has been shown to produce no other results other than a significantly lower average lung lesion score following a challenge with a dose of 1.0×10^6 wild-type *Mycoplasma hyopneumoniae*. No other route of administration other than the intramuscular route of administration of the MHDCE vaccine plus adjuvant mixture is used in the instant specification. This is important since the first trial described on pages 16 and 17 and Table 1 of the instant specification reflects unpredictability in the protective ability of art-available *Mycoplasma hyopneumoniae* bacterin, such as, Ingelvac *M. hyo*® which did not elicit a significant decrease in average lung lesions. Additionally, the claimed

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method has been shown to be operative at one challenge dose, but not at the other. As shown via the second trial on pages 13 and 14 of the specification, a single dose of the vaccine of Example 2 (i.e., MHDCE plus the recited adjuvant) administered intramuscularly showed significantly lower average lung lesions compared to the challenge control animals only at a challenge dose of 1.0×10^6 *Mycoplasma hyopneumoniae*, but not at a dose of 1.4×10^6 *Mycoplasma hyopneumoniae*. The only "animals" that are used in these experiments are pigs. These issues are critical since the art reflects that bacterial killed vaccines (bacterins) vary in their immune response based on the route of immunization. For instance, George *et al.* (*Microbiol. Immunol.* 33: 479-488, 1989) taught the route-related variation in the immunogenicity of killed bacterial vaccines due to variation in the presentation efficiency of macrophages or other antigen presenting cells (see page 479 of George *et al.*). George *et al.* showed that a bacterial killed vaccine was not only non-immunogenic by intraperitoneal route, but that immunization with a killed bacterial vaccine by intraperitoneal route even resulted in immune suppression. See abstract of George *et al.* The art further reflects that the degree of protection obtained in a protection/challenge experiment conducted under laboratory conditions depends on the route of administration, the frequency of administration, the adjuvant(s) used, the dose of challenge and the interval of challenge. The protection experiment carried out in a laboratory does not simulate the naturally occurring infections. The art reflects the difficulty in carrying out protection experiments against enzootic pneumonia in the laboratory and the inability to produce enzootic pneumonia uniformly in naturally-born control pigs. See page 462 of Goodwin *et al.* (*Brit. Vet. J.* 129: 456-464, 1973 - Applicants' IDS). It has been recognized in the art that the success of a protection experiment depends on the type of pigs used in the experiment and the method of challenge. See page 462 of Goodwin *et al.* The extent to which laboratory protection experiments indicate effectiveness against natural *M. suis* disease is stated to be not known in the art. See page 462 of Goodwin *et al.* The art indicates that the conditions under which laboratory protection experiments are conducted do not appear to meet the field conditions. It is also taught that a vaccinated animal which resolves its lung lesions might not resist natural infection. The art recognizes that a reduction in lung lesions is not equivalent to protection *per se*, or to cessation of

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economic loss. See page 462 of Goodwin *et al.* In the instant case, what is characterized as 'protection' is limited to a showing of statistically significant numerical reduction in average lung lesions in pigs vaccinated with MHDCE and the recited adjuvant mixture and experimentally infected with 1.0×10^6 *Mycoplasma hyopneumoniae*, but not in those animals which were challenged with 1.4×10^6 *Mycoplasma hyopneumoniae* after a single intramuscular immunization with the recited vaccine.

Because of the art-demonstrated unpredictability in demonstrating protection in any animal against natural infection with *Mycoplasma hyopneumoniae* under field conditions using any bacterin preparation of *Mycoplasma hyopneumoniae* by any route and against any challenge dose, the enablement of representative numbers of bacterins of *Mycoplasma hyopneumoniae* administered via a representative number of routes of administration in a representative number of different animals is critical for one of ordinary skill in the art to reproducibly practice the full scope of the instantly claimed method. The entire scope of the instant claims is viewed as being non-enabled for reasons set forth above. Undue experimentation would have been required by one of ordinary skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of specific disclosure and specific guidance, the lack of specific working examples enabling the entire scope, the demonstrated unpredictability as reflected in the specification and in the state of the art at the time, the quantity of experimentation necessary, and the breadth of claims.

Remarks

- 7) Claims 10-17 stand rejected.
- 8) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

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9) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December, 2002

S. DEVI, PH.D.
PRIMARY EXAMINER